UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/632,149	08/03/2000	R. Andrew Cuthbertson	A-59553-2 DAV JJD	1941

7590 01/19/2002

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
2632	12

DATE MAILED: 01/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Advisory Action	Application No.	Applicant(s)	
	09/632,149	CUTHBERTSON, R. ANDREW	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 21 November 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 21 November 2001. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: 13-22.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☑ Other: IDS 1449 #5

Continuation of 5. does NOT place the application in condition for allowance because: Applicants' arguments are found to be unpersuasive for overcoming the rejection of record with regard to the following issues:

(1) With respect to the issue of treating a genetic ocular disease, Applicants argued that the claimed invention does not require curing or stabilizing a genetic ocular disease, and that it is not necessary to demonstrate curing a genetic ocular disease in order to demonstrate alleviating symptoms of a genetic ocular disease. Applicants further argued that a method of treating a degeneration of ocular cells as a result of a genetic disease so as to alleviate the degeneration of the ocular cells which is acknowledged to be enabled by Examiner can include the curing a genetic ocular disease. It is noted that the term "treating" is not defined in the instant specification. As well known in the art, treating a disease encompasses curing, stabilizing, slowing the progression of the disease and alleviating symptoms associated with the disease. As such, the instant specification is not fully enabled for the entire scope of treating a genetic ocular disease or an ocular disease in the methods as claimed. This is because even many years after the effective filing date of the present application, with respect to gene therapy for ocular disease Bennett and Maguire (Mol. Therapy 1:501-505, 2000, Cited previously) stated that "[t]here has not, as yet, been a demonstration of cure using gene therapy approaches..." (page 501, col. 1, middle of the first paragraph), and "There is currently no cure for retinitis pigmentosa and existing treatments are of uncertain or limited benefit in retarding the progression of the disease" (page 502, col. 2, middle of first full paragraph). Additionally, it is highly unlike that a cure, a stabilization or retardation of the progression of an ocular disease via gene therapy is achievable because it is well recognized in the gene therapy art that there is a lack of a long term and stable therapeutic transgene expression in vivo as evidenced by the teachings of Bennett et al. (Nat. Med. 2:649-654, 1996; Cited by Applicants previously) and Dang et al. (Clin. Cancer Res. 5:471-474, 1999; Cited previously). Bennett et al. stated that "The ability to interfere with retinal degeneration in humans will depend on the stability of the transduced genes. Ideally, for application to the slowly progression human diseases, the transgene-expressing cells should persist over years or even decades. Although we have observed transgene expression in transduced retinal cells at least 100 days after injection, the number of expressing cells diminishes with time (page 652, col. 2, top of the first full paragraph). Moreover, with respect to Norrie's disease, blue cone monochromasy and choroideremia, although genetic mutations have been identified, there is no evidence indicating the correlation between the identifed mutations and the cause of the diseases at the effective filing date of the present application. Furthermore, the scope of the claims o encompasses treating genetic ocular diseases in which specific genetic components are still unknown, for examples age-related macular degeneration, anterior and posterior uveitis, retinovascular diseases, cataracts, corneal dystrophies, retinal detachment among others. As such, with the lack of guidance provided by the present disclosure regarding to the specific vector constructs comprising specific transgenes utilized to treat the aforementioned genetic ocular diseaes, and given the state of the art it would require undue experimentation for a skilled artisan to make and use the methods as claimed. It should be further - noted that the scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art.

To alleviate the degeneration of the ocular cells as a result of a genetic ocular disease is not the same or equivalent to cure a genetic ocular disease via gene therapy for the reasons set forth above. The post-filing arts of record all indicate a delayed in photoreceptor cell death via the utilization of recombinant expression vectors expressing wild type cGMP phosphophodiesterase or bFGF or ciliary neurotrophic factor, but it does not indicate that the genetic defects have been corrected or the symptoms associated with the genetic ocular diseases are no longer present in the treated animals.

(2) With respect to the issue of methods of gene delivery into in situ ocular cells, Applicants argued that "the specification provides one of skilled in the art with a variety of methods to incorporate an exogenous nucleic acid into an ocular cell, and with methods for determining conditions permissive for the uptake of the exogneous nucleic acid. Further, the specification is not required to teach every condition that is permissive for the uptake of exogenous nucleic acids into ocular cells". Therefore, Applicants assert that the specification is fully enabled for the scope of the methods as claimed. Examiner noted that the disclosed routes of incorporating exogenous nucleic acid into an in situ ocular cells such as direct application of an exogenous nucleic acid to the surface of ocular cells, injection of an exogneous nucleic acid into the eye and bolistic nucleic acid delivery into the eye are all encompassed within the scope of direct administering an exogenous nucleic acid into an in situ ocular cell which is already acknowledged to be enabled. However the claimed methods encompass both direct and systemic administration of an exogenous nucleic acid into an in situ ocular cell to achieve therapeutic effects contemplated by Applicants for treating a genetic ocular disease. Even many years after the effective filing date of the present application (10/31/1994), Bennett and Maguire (Mol. Therapy 1:501-505, 2000; Cited previously) stated that "Systemic delivery of gene therapy agents does not result in gene delivery to ocular structures" (page 501, col. 1, first sentence of second paragraph). Furthermore, it is also well known in the art that the major challenge limiting the effectiveness of gene therapy is the lack of an efficient and effective gene delivery to targeted cells or tissues. Vector targeting in vivo to desired cells or tissues is unpredictable and inefficient, and the resolution to vector targeting in vivo had not been achieved at the effective filing date of the present application as evidenced by the teachings of Verma & Somia (Nature 389:239-242, 1997; Cited previously) and Dang et al. (Clin. Cancer Res. 5:471-474, 1999; Cited previously). With the lack of guidance provided by the present disclosure, it would require undue experimentation for a skilled artisan to make and use the methods as claimed. Moreover, the Appeal courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in the patent application (27 USPQ2d 1662 Ex parte Maizel.).

DAVE T. NGUYEN
PRIMARY EXAMINER